Grey Literature Data Extraction

EFSA report "Scientific expert opinion on the public health risks of bacterial strains producing extended-spectrum B-lactamases and/or AmpC B-lactamases in food and food producing animals"

Key findings:

- The predominant ESBL families encountered in food and food-producing animals are CTX-M, TEM and SHV. The predominant AmpC family is CMY. The bacterial species that most commonly produce ESBLs are Escherichia coli and non-typhoidal Salmonella (serovars S. Typhimurium, S. Newport and S. Heidelberg).
- Data on prevalence of cefotaxime resistance (used to determine presence of ESBL genes in Salmonella and E. coli) in meat is limited. Belgium and the Netherlands reported high to moderate levels of cefotaxime resistance in salmonella and E. coli in poultry meat. There has been an increase in ESBL- and AmpC producing E coli and salmonella in food in Europe and globally. Poultry products seem to be the ones carrying the highest levels of these bacteria.
- Transmission of ESBL genes, plasmids and clones from poultry to humans is most likely to occur through the food chain, based in recent evidence.
- The establishment of risk factors for occurrence of ESBL/ AmpC producing bacteria is complicated due to the lack of (accurate) data. Use of antimicrobials in and trade of animals of EU countries with the few countries that lead production and export of breeding animals are risk factors for the occurrence and spread of ESBL/ AmpC producing bacteria, but there is lack of data at that level of production though it has been observed that ESBL and AmpC producing E coli have been introduced in poultry production chains through day 1 old grandparent chicks.
- Recommendations from this expert opinion included:
    - Stop all uses of cephalosporins/ systematically active 3rd and 4th generation cephalosporins or to restrict their use (only allowed under specific circumstances). Minimise off-label use by increasing compliance with existing legislation.
    - Control dissemination of these organisms by
        - increasing farm biosecurity
        - impose controls on animal trade (of ESBL/AmpC carriers)
        - improving hygiene across the food chain
        - implementing other general post-harvest controls for foodborne pathogens
    - There are currently differences in the MIC breakpoints defined for ceftazidime, cefoxitin, and cefepime (3rd and 4th generation cephalosporins) which are still one to two dilution steps higher for CLSI compared to those used by EUCAST. For the optimal harmonisation of the interpretation of susceptibility data and for phenotypic detection of ESCL and/or AmpC producers, it is important to use EUCAST clinical breakpoints for interpretation of susceptibility or resistance and EUCAST epidemiological cut-off values (ECOFFs) to determine if an isolate belongs to the wild-type population or not.

Scientific Opinion on Carbapenem resistance in food animal ecosystems (BIOHAZ)- EFSA journal 2013; 11(12): 3501

Key findings:

No major findings provided, all were in line of recommendations.

Recommendations:

- EFSA currently recommends on their technical reports that mandatory phenotypic monitoring of Salmonella spp and indicator E coli with a broadened test panel including meropenem susceptibility testing. Furthermore, active monitoring and/or additional targeted surveys for carbapenemase producing bacteria in food should cover key zoonotic agents and indicator organisms of the commensal flora. Active and passive monitoring and/or targeted surveys should cover key zoonotic agents, animal pathogens and indicator organisms. Priority should be given to meat derived from broilers, fattening turkeys, fattening pigs and veal calves. Raw milk and aquaculture also to be included in targeted surveys. Active monitoring of all isolates of Salmonella spp and E coli collected within the compulsory monitoring program as required by European legislation should be screened for meropenem resistance following standardised microdilution methods;
- Sampling strategy (active vs passive monitoring) and selection procedure for each isolate (randomly selected isolate versus isolate from selective media) should always be provided for the correct interpretation of results related to carbapenem resistance;
- Phenotypic results should be substantiated with methods used for assessing carbapenemase production, findings of characterisation of resistance genes should be provided for each isolate.
- Pre-enrichment methods should be used in specific surveys to increase sensitivity for populations with low prevalence of carbapenemase-producing bacteria.
- The choice of selective media for the surveillance of carbapenem resistance for testing food samples needs to be experimentally evaluated and validated as these are currently not available;
- Plasmid and strain typing should be undertaken to acquire better knowledge on the epidemiology of genes encoding carbapenemase production among bacteria from food derived from production animals;
- Ban on the use of carbapenems in food-producing animals to be continued in the EU and in other countries.
- Decrease use of antimicrobials in animals production in the EU in accordance with prudent use guidelines is of high priority
- Effectiveness of interventions to be monitored through targeted surveys of food, selective isolation methods and pre-enrichment of samples.
- Control measures to be proactively implemented at national and international levels to prevent carbapenem-resistant strains to become widespread in livestock

EFSA Public health risks associated with Enteroaggregrative Escherichia coli (EAEC) as a food-borne pathogen (EFSA journal, 16th December 2015)

Note- these were pathogenic strains of E coli, not commensal bacteria.

EFSA Scientific Opinion on monitoring and assessment of the public health risk of "Salmonella Typhimurium-like" types, EFSA journal 2010; 8(10):1826

Key findings:

- Monophasic variants of S. Typhimurium (1,4[5],12:i:-) appear to be increasing in many EU member states and can cause infection in humans and food-producing animals (Note- but no mention was made in the scientific opinion about food);
- Monophasic S. Typhimurium strains have been shown to have similar virulence and antimicrobial resistance characteristics to strains of S. Typhimurium. Many of the clonal likes of monophasic S. Typhimurium are multidrug resistant and exhibit resistance to commonly used antimicrobials

Recommendations:

- Antimicrobial susceptibility testing should be conducted and reported in a harmonised way for human, animal and food isolates, according to European guidelines.
- It is important to monitor the further spread of monophasic variants of S. Typhimurium; there seems to be a particular lack of evidence for monitoring of these in poultry flocks in many EU Member States (Note- no information provided for evidence and gaps of knowledge for food products).

EMA report "Answers to the requests for scientific advice on the impact on public health and animal health of the use of antibiotics in animals", 18th December 2014, EMA/381884/2014, Veterinary Medicines Division/CVMP/CHMP. 83 pages

Key findings:

- There is currently evidence that reduction of use of critically important antimicrobials (CIAs), particularly of 3rd and 4th generation cephalosporins and fluoroquinolones causes reduction in the occurrence of resistance to such antimicrobials in *E. coli* isolated in poultry meat in countries where policies to reduce AMU have been implemented. Most of these evidence is from Scandinavian countries and from the Netherlands.
- The effects of voluntary or compulsory withdrawal of cephalosporins for use in food animals in several EU Member States have not been assessed.

Recommendations (Note: these were mainly focus on AMU, so not extracted):

- More information is needed on the off-label use of critically important antimicrobials before an assessment can be made of any risk this may have for AMR emergence.
- Third and fourth generation cephalosporins not to be used in poultry due to the potential selection of ESBL-producing bacteria and transmission to humans through food (poultry meat)
- Further research is required on
    - the pathways for dissemination of antimicrobial resistant bacteria from animals to food;

- methods for the quantification of the spread of resistance genes from commensal; to pathogens in food and the environment

Tackling antibiotic resistance from a food safety perspective in Europe. World Health Organisation, Regional Office for Europe. Denmark. 88 pages. 2011

Key findings:

- Overuse of antimicrobials in food-producing animals has important consequences for public health as it promotes the emergence of antimicrobial-resistant bacteria and resistance genes that can be transfer to humans often through consumption of food but also through direct contact with animals or environmental mechanisms.
- Resistance in foodborne zoonotic bacteria Salmonella and Campylobacter is clearly linked to antibiotic use in food animals, and foodborne diseases caused by such bacteria in humans are well documented; of special concern is the occurrence of resistance to critically important antimicrobials;
- In cases of human infections caused by multidrug resistant S. Typhimurium DT104 resistant to quinolones therapeutic failure, increased hospitalisation and higher risk of death has been reported.
- In human cases caused by macrolide-resistant Campylobacter strains, these are more likely to cause invasive illness and death compare to infections caused by susceptible strains.

Recommendations:

- Tackling antimicrobial resistance requires a holistic, intersectoral and multifaceted approach with effective coordination of action and exchange of information among the agricultural, food, veterinary and health sectors. International cross-collaboration is essential but countries should also take a national approach to antimicrobial resistance and food safety. This calls for the establishment of a formal mechanism of interaction between the health ministry and other relevant ministries and authorities to address antimicrobial resistance in the food chain.
- Use of antimicrobials in food-production animals:
    - Use of antimicrobials as growth promoters (AGPs) to be banned;
    - Antimicrobials to be used in animals only when indicated and prescribed by veterinarians;
    - Critically important antimicrobials (fluoroquinolones, 3rd and 4th generation cephalosporins) only to be used in food-producing animals when its use is justified
    - Antimicrobial use should only be used for therapeutic purposes and as little as possible
        - National veterinary, agricultural and pharmaceutical companies should promote preventive veterinary medicine (e.g., disease prevention including development of effective vaccines) and prudent use of antimicrobials in collaboration with the private sector and all relevant stakeholders, particularly practitioners and farmers;

        - The Codex Alimentarius and OIE have developed guidelines for the prudent use of antimicrobials in food-producing animals.
        - The WHO (together with OIE and FAO) has developed the WHO Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food included in the WHO Global Strategy for Containment of Antimicrobial Resistance;
    - Improvement of biosecurity measures, good hygienic and management practices;
    - Eliminate economic incentives that facilitate inappropriate prescription of antimicrobials.
- Surveillance efforts:
    - Implement surveillance systems to monitor AMU in humans and food-producing animals;
    - Establish an integrated surveillance system involving public health, food and veterinary sectors to monitor AMR in selected foodborne bacteria
- Advocacy and communication activities are required to raise awareness for AMR from a food safety perspective and to prompt action that prevents its development and spread in the food chain.
- Veterinary, agriculture and food authorities should consider the development of guidelines on the prudent AMU in food-producing animals, taking a multidisciplinary approach. These guidelines should cover the use of critically important antimicrobials for human medicine. The competent authorities should also provide adequate training required for the implementation of these guidelines.
- National authorities, together with the private sector should support studies to help provide comparable data on AMR and AMU for risk assessment and risk management.
- Support to be provided to strengthen research on the development and spread of resistance, and the development of new antimicrobials and alternative approaches to antibiotic therapy.

UK One Health Report. Joint report on human and animal antibiotic use, sales and resistance. Hopkins, S and Muller-Pebody B. 64 pages.

<u>Key findings</u> (Note: although AMR patterns were provided for human and animal isolates, these were not reported for foods):

- There were many caveats surrounding the interpretation of data presented in the report as the methods of data collection varied to such an extent that they couldn't be meaningfully compared

<u>Recommendations</u>:

- PH organisations to work with professional organisations to develop guidance related to recommended antibiotic and bacterial combinations, which should be tested and reported by clinical laboratories for key One Health pathogens.

- Animal health organisations should review the antibiotics tested from clinical veterinary samples and through the EU harmonised monitoring in animals to align with key antibiotics required for human treatment.
- The Veterinary Medicines Directorate (VMD) will conduct carbapenem resistance monitoring (as part of the EU monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria in accordance with the EU legislation, Commission Decision 2013/652/EU), a year earlier than mandated.
- VMD will participate in the protocol development of the European Surveillance Veterinary Antimicrobial Consumption (ESVAC) project to collect farm level data from the pig sector; and investigate and facilitate options for collecting accurate antimicrobial consumption data at an individual farm level;
- Public and professional One Health activities should be enhanced through engagement with the European Antibiotic Awareness Day (EAAD) campaign and aligning programs for human and animal health professionals;
- Human and animal surveillance bodies should produce a further report in two years, encompassing robust data collected by the FSA on the burden of AMR in imported food animals.

Side report for context:

ACMSF 1999. Report on Microbial Antibiotic Resistance in Relation to Food Safety.

Key findings:

- the extent to which giving antimicrobials to animals contributes to the overall problem of bacterial antimicrobial resistance in humans is uncertain and the evidence and information needed to resolve the uncertainty is lacking.

- Studies on the emergence of bacterial resistance in animals given antimicrobials are few, and scarce research has been done in the transmission of resistant bacteria in food to humans.

- There was too little effort put into investigating the incidence and prevalence in bacteria in food animals;

- International trade of food is likely to contribute to the dissemination of resistant bacteria. There is little scope in banning AMU in the UK whilst importing food with its bacteria from countries where these bans are not imposed.

- High prevalence of MDR strains of S. Typhimurium DT104 and evidence of food-associated infections in humans. There is also PH concerns on other resistant strains of Salmonella.

- Emergence of quinolone resistance in Campylobacter bacteria; campylobacter is the most common agent involved in foodborne disease in humans in the UK. Poultry meat is a known reservoir for *C. jejuni* and *C. coli*. Emergence of (fluoro)quinolone resistance is of major concern as these antimicrobials are used to treat infections caused by Gram-negative and Gram-positive bacteria in humans. Widespread usage of enrofloxacin in the poultry industry has been noted; for this, veterinary use of these antimicrobials could be involved in the emergence of quinolone-resistance in Campylobacter bacteria.

- therapeutic and prophylactic use of antimicrobials of importance in the treatment of human infections

- EU consideration for the ban of AGPs in food-producing animals;

- Metaphylactic use of antimicrobials in groups of food-producing animals and poultry as an intervention to prevent the spread of infectious diseases in veterinary medicine compared to human medicine;

- Role of antimicrobials in modern aquaculture production. Previous, high AMU to tackle infectious bacterial diseases in fish had been reported in this sector. It was acknowledged that the development of vaccines and improved husbandry practices has reduced AMU in this sector. It is expected that the aquaculture industry will continue to adopt these approaches when developing farming of seabass and seabream. However, the Committee recognised that the issue with AMR in aquaculture will continue in countries (particularly those outside the EU) where antimicrobials are used extensively for therapeutic and prophylactic purposes. A similar situation is observed in ornamental fish, for which evidence of MDR bacteria has been noted.

- Possibility that imported foods might be more likely to contain antimicrobial resistant organisms that domestically-produced food due to the freer availability of antimicrobials to agricultural producers in other countries

- use of antimicrobial markers in genetically-modified food organisms.

- the panel recognised that the contribution of antimicrobials used in animal food production to AMR in humans may be small compared to that by use of antimicrobials in the community and general practice. Nevertheless, AMU in food-producing animals can lead to the emergence of AMR that can spread to humans.

- there is no compelling evidence that there is widespread microbial antimicrobial resistance in food-producing animal populations. This reflects a paucity of surveillance and research specifically focusing on AMR.

- AMR in food-producing animals is derived from AMU in the farm environment and current husbandry practice. This is the origin of resistant Salmonella and Campylobacter bacteria observed both in animals and humans; it is recognised that transfer of resistant bacteria from animals to humans may occur through food chain exposure pathways and the occurrence of this through direct contact with food-producing animals is also acknowledged.

- ACMSF welcomed the creation of the Responsible Use of Medicines in Agriculture (RUMA) that will develop guidelines for the livestock industry to reduce its reliance of antimicrobials.

- Disposal of farm effluents, sewage sludge and abattoir waste to pasture and agricultural land could have a role in the dissemination of resistant bacteria to livestock and human populations.

- Companion animals are also acknowledged to contribute to the issue of AMR, and can act as reservoirs, transferring to humans through close contact. AMU in ornamental fish is perceived to be a risk through direct contact exposure.

<u>Recommendations</u>:

- More and better research and surveillance studies are needed to ascertain the extent to which AMU in animals results in antimicrobial resistance in bacteria in humans.

- Improve our understanding of resistance in bacteria isolated from food animals and foodstuffs, of human infections associated with antimicrobial resistant foodborne pathogens, and of ways in which the food chain contributes to human infections with antimicrobial resistant microorganisms;
- Reduction of AMU to be applied in suitable, effective alternatives are in place, particularly when AMU is used as a "replacement" for hygienic animal husbandry. Livestock industry to accept that good farming practices are likely to reduce the need for AMU. Also use of alternatives to AMU include the adoption of Hazard Analysis Critical Control Point (HACCP) principles to ensure food safety from farm to fork;
- A multidisciplinary liaison group to be set up to monitor developments in bacterial resistance to antimicrobials with the aim to identify action which could be taken on a co-ordinated basis to address any emerging trends;
- WHO's meeting on the use of antimicrobials in animal feed in 1997 stated that:
    - antimicrobials should not be used for growth promotion purposes if these are used in humans for therapeutic purposes or known to select for cross-resistance to antimicrobials used in human medicine in line with the Swann Committee made in 1969. Therefore, the ACMSF committee considers that the use of drugs such as spiramycin, tylosin phosphate and virginamycin should be discontinued as AGPs (this was requested by the ACMSF committee to the Minister of State at MAFF; the EU Agriculture Council decided on the 14th of December 1998 that bacitracin zinc, spiramycin, tylosin phosphate and virginamycin should be suspended from 1st January 1999). Remaining drugs to be continued to be used as AGPs (avilamycin, bambermycin, bacitracin zinc, monensin sodium and salinomycin) should be closely controlled for its potential implications for PH. In addition, olanquidox, copper and zinc (that can also be used as AGPs) should be monitored for potential role in selection for AMR. No new substances should be developed for use as AGPs if these have possible applications in human clinical treatment;
    - National authorities should define threshold levels of resistance in bacteria and circumstances where mitigation strategies should be instigated and if such procedures are unsuccessful, when approval should be withdrawn;
    - No antimicrobial should be administered to a food-producing animal unless it has been evaluated and authorised by the competent authorities. Evaluation should include a risk assessment (including the development of resistance which may impact public health) and a post-marketing monitoring programme to detect the emergence of resistance of public health significance. If emergence is detected, appropriate action should be taken which may include the withdrawal of the antimicrobial in question
- WHO meeting in 1998- use of quinolones in food-producing animals and impact on PH:
    - Recommended that research on quinolone resistance should be conducted
- House of Lords 1998 "Report on Resistance to Antibiotics and other Antimicrobial Agents" called for:
    - Voluntary phasing out of use of virginiamycin for growth promotion
    - Code of Prescribing Practice for veterinarians
- House of Commons Report on "Food Safety" 1998 called for:
    - Total ban on antimicrobials for growth promotion purposes;
    - Tighter restrictions for AMU for sub-therapeutic or prophylaxis purposes in food-producing animals.

- Different kind of markers (non-antimicrobial) should be used in genetically modified food organisms.
- Implications of the appearance of local pockets of resistance should be raised at a higher level of debate:
    - Pharmaceutical companies are to monitor where resistance arises and report to the licensing authorities on specific instances and trends. This information should form the basis for licensing authorities to rescind or not to authorise product licenses when AMU in animals is seen to compromise the treatment of human disease;
- Disposal routes of farm and abattoir waste merit further investigation due to the potential role in AMR transmission
- Tighter controls to be implemented for medicated animal feedingstuffs. Feedingstuffs for food producing animals are to be manufactured, stored and distributed in a safe and professional manner, following the various Codes of Practice and Guidelines. Those engaged in feed production should implement HACCP to their operations. The Government should review the arrangements under which discarded medical additives can be re-used in medicated feed (Note: ACMSF committee noted their reservations on this issue).
- in countries (particularly those outside the EU) where antimicrobials are used extensively for therapeutic and prophylactic purposes in aquaculture, continued vigilance is needed (this is also applicable to ornamental fish);
- Improved detection of AMR bacterial strains, microbiological risk assessment, improvement, pathogenicity and clinical outcomes, microbial physiology and ecology, and mechanisms of resistance and dissemination of resistance determinants is required.

As published in the recommendations section in the report:

- The Government should:
    - start studies to identify the key factors for the emergence and disappearance of MDR clones of S. Typhimurium observed in food-producing animals (M/L effect)
    - ensure that isolates from salmonellas from animals in England, Wales, Scotland and Northern Ireland are compared using suitable methodologies in order to detect any geographical variations in antimicrobial susceptibilities (M/L effect).
    - Consider how monitoring of pathogens in food-producing animals can be improved in order to obtain data on prevalence, subtypes and AMR in important foodborne pathogens and publish this information on a regular basis (M/L effect);
    - Organisations directing or undertaking surveillance of organisms isolated from animals should work together with organisations monitoring resistance in bacteria from food and humans (and vice-versa) to produce an annual UK report summarising AMR in the food chain (M/L effect);
    - Investigate the basis for regional differences in fluoroquinolone resistance in salmonellas in the UK in human infections via foodborne route (ML effect);
    - Seek ways of achieving further standardisation of AMR testing across Europe and internationally (human infections via foodborne route) (M/L effect);
    - In association with other Member States of the European Union, should require applicants applying for marketing authorisations for antimicrobials for veterinary use to supply data derived from the testing of the antimicrobial concerned for AMR in target animal species under intended conditions of use. Such data should be made publicly available in support of lincensing decisions (Imm effect);

- Discuss with the veterinary profession and the pharmaceutical industry ways in which the information gathered through post-marketing surveillance, including that of incidence and prevalence of AMR, could best be available to the veterinary and medical professions. Regulatory authorities to give high degree of attention to the AMR issue both in the initial licensing process and subsequently at the 5 year license review stage (Imm effect);
- To establish amounts of antimicrobials given to food-producing animals. This information should be published at regular intervals by the Veterinary Medicines Directorate and should be structured as to provide a breakdown by compound, class, medical equivalent (where appropriate) and target (Imm effect);
- Coordinate a strategy for the reduction of AMU in food-producing animals;
- Ensure that all antimicrobials used for purposes other than growth promotion are prescribed only medicines (POM) in food-producing animals (Imm effect);
- Ensure that all prescribing by veterinarians is for animals under their care (Imm effect);
- Ensure that detailed written justification is provided by veterinarians using Cascade medicines (off-label use) (Imm effect);
- Bring together the relevant bodies to produce and publish without delay (Imm effect):
    - Codes of Practice aimed and reducing AMU;
    - Appropriate dosage strategies;
    - Detailed preventative medicine programmes for all livestock-based food production enterprises covering routine medication (including AGPs and anticoccidials), length of treatment regimens, competitive exclusion and probiotic treatments and vaccines;
    - Policies and protocols for the use, storage and disposal of antimicrobials;
- Mount regular campaigns to remind livestock industry of its statutory obligations in respect of the maintenance of farm medication records, to improve enforcement, and to greatly enhance current performance levels (Imm effect);
- Carry out regular, statistically-robust, compliance surveys and should review existing arrangements to ensure that effective follow-up action can be taken where non-compliance is identified (M/L effect);
- Encourage use of HACCP as a tool to improve farm practice and as a means of ensuring the responsible AMU, thus tackling AMR;
- Encourage regular veterinary visits to all livestock farms or production units to audit animal disease profiles and general performance indicators, to accumulate and scrutinise mortality, morbidity and general health data and to record AMR patterns so that AMU can be adjusted accordingly (Imm effect);
- Require regular on-going surveillance of a representative cross-section of commercial feed compounders, integrated poultry producers and on-farm mixers to test compliance with the law and to oversee the guidelines for ensuring that medicated feeds intended for food-producing animals are manufactured, stored and distributed in a safe and professional manner (Imm effect);
- Review the adequacy of the current frequency of inspections by the enforcement bodies for medicated feedingstuffs (Imm effect);
- Review the arrangements under which discarded and surplus medicinal additives may be re-used in medicated feed and medicated pre-mixes with a view to phasing

out this practice in favour of appropriate disposal as waste material at the earliest opportunity (Imm effect);
    - License the use of antimicrobials in new fish species being developed for aquaculture for a short a period as is feasible and equitable (Imm effect);
    - Issue public advice warning of the potential risk of the transfer of AMR bacteria through direct contact exposure to ornamental fish;
- Reference laboratories:
    - To establish relationship between AMR and subtype of animal isolates of Campylobacter to aid further studies aimed at identifying sources of resistant strains (M/L effect);
    - Those for enteric pathogens in the UK, labs should consider screening these and other microorganisms isolated from routine food samples for AMR and publish their data on a regular basis (M/L effect);
    - Carefully examine the relationship between AMR and subtype of human isolates of campylobacter to aid further studies aimed at identifying the sources of antimicrobial resistant strains;
- UK veterinary laboratories/ UK Food laboratories/ UK clinical laboratories:
    - Surveys to be conducted to ascertain current practices with regards to AMR testing of microorganisms important in the food chain with a view to improve the comparability between animal, food and human data (M/L effect).
- VLA (APHA) to consider:
    - Inclusion of E. coli in any surveillance of AMR in "healthy" food-producing animals (M/L effect);
    - Collate and publish its data on resistance in anaerobes in food-producing animals at the earliest opportunity (M/L effect);
- There should be enhanced national and international surveillance for AMR of microorganisms isolated from food. When planning future food microbiological surveys, consideration should be given to the screening of foodborne pathogens and other microorganisms for AMR using appropriate methodology (M/L effect);
- Using appropriate methodologies, *E. coli* isolates from foodstuffs should be screened for AMR to provide a more sensitive indication of differences between food commodities and changes in resistance over time (M/L effect);
- Continual surveillance and assessment of risks to humans associated with use of AGPs still authorised in the EU should be implemented;
- Veterinary profession (food chain):
    - To address over-use of fluoroquinolones (Imm effect);
    - Codes of practice for prescription of antimicrobials to be introduced asap (Imm effect);
- Studies to be conducted to:
    - Gather further data on AMR in campylobacters in the UK in food (M/L effect)
    - Explore the variability in the isolation of resistant campylobacters from retail poultry in several studies (M/L effect)
    - The relative contribution of meats, dairy products, raw vegetables and fruits as vehicles for antimicrobial resistant enterococci should be clarified (L/M effect);
- Research funding organisations should:
    - Undertake studies to assess effect of food processing, storage conditions and food preparation on the antimicrobial-resistant flora of foods and the transfer of resistance between food bacteria (M/L effect);

- Commission research to establish why certain Salmonella serotypes (e.g., S. Hadar, S. Typhimurium, S. Virchow) develop AMR and MDR, where others (S. Enteritidis) remain largely sensitive in human infections by foodborne route (M/L effect);
- Research should be funded to (M/L effect):
    - Undertake integrated local surveillance studies to examine the prevalence of AMR with Campylobacter, Salmonella and commensal bacteria in red meat and poultry through slaughter and processing;
    - Assess the prevalence of AMR in wild animals, including birds, and food-producing animals in relation to AMU, particularly AGPs and fluoroquinolones;
    - Identify risk factors for acquiring an infection with a AMR foodborne pathogen. Such studies should be conducted both in humans, and where appropriate, in animals;
    - Assess extent of infection in travellers caused by AMR strains and the contribution of these make to the burden of IID and AMR in the UK;
    - Assess importance of imported food and animal feed as a source of AMR bacteria;
    - Determine the contribution made by microorganisms of human origin to AMR in animals and food;
    - Model current patterns and predict future trends in AMR of foodborne pathogens in humans and animals;
    - Determine the socio-economic costs attributable to AMR foodborne pathogens in humans, above the costs attributable to antimicrobial-sensitive foodborne pathogens;
    - To develop methods which will characterise the origins of resistance in foodborne pathogens and commensal microorganisms, so as to improve identification of the sources and routes of transfer of AMR organisms from the farm through food to humans (M/L effect);
    - Microbiological risk assessment (MRA) (M/L effect):
        - Undertake structured MRA to assess the risk of infectious intestinal disease from AMR foodborne pathogens and commensal bacteria in food-producing animals, foods and the environment;
        - Use MRA to quantify the magnitude of the key pathways by which AMR can transfer from food-producing animals to humans via the food chain and the environment;
        - Undertake MRA to assess the links between AGPs and fluoroquinolones use in food-producing animals and the development of AMR infections in humans;
    - In order to reduce AMU:
        - Underpin effective antimicrobial management policies in animals, aimed at optimising administration practices to minimise the risk of development of AMR. This will include investigations of the persistence of AMR bacteria in the gastrointestinal tract of food-producing animals after antimicrobial withdrawal;
        - Further investigate how particular hygiene practices and interventions can bring about a reduction in the need for antimicrobials in food-producing animal production, without compromising animal welfare;

    - Evaluate the potential of vaccines, probiotics and competitive exclusion to reduce AMU and the level of resistance in microorganisms in food-producing animals;
    - Determine the relationship between AMR and virulence in foodborne pathogens in humans and, and where appropriate in animals;
    - Review the clinical picture (duration, severity, treatment and outcome) of cases of IID involving AMR foodborne pathogens as opposed to cases caused by sensitive isolates, and assess whether there are any longer-term consequences of these infections for the patient;
    - Examine AMR pathogens and commensal organisms from animals and humans to determine their survival characteristics in the environment, compared to non-resistant strains;
    - Examine the effect of antimicrobial selection pressure on the survival and persistence of AMR strains, both in vitro and in vivo;
    - Examine the transfer of resistance determinants between foodborne pathogens and the commensal flora of humans and animals in foods and the environment;
- The BVA and other relevant professional representative bodies in cooperation with veterinary schools and colleges, the farming industry and others, should develop appropriate courses to better inform veterinary prescribing and AMU and to draw attention to the potential dangers of resistance (Imm effect);
- Veterinary schools and colleges should review their existing courses to ensure that AMR is given a suitably high profile in undergraduate training (Imm effect);
- For medicated feedingstuffs, on-farm mixers using medicinal additives and intermediate medicated feedingstuffs in any manner should be required to register with the RPSGB or DANI (Imm effect);
- Manufacturers that fail to comply with UKASTA's Feed Assurance Scheme should not be regarded as suitable for registration by the enforcement authorities. Also, those engaged in the manufacture of medicated animal feedingstuffs are strongly encouraged to apply HACCP to their operations, not only for commercial feed compounders and the integrated poultry producers but for on-farm mixers too (Imm effect).